

I claim:

1. A method for preparing a stable, retroviral packaging cell line for generation of human serum-resistant retroviral vector particles (RVP) which comprises

(a) introducing one or more packaging vectors into a non-primate mammalian cell line, wherein said cell line exhibits (substantially) no hybridization to a Moloney-MLV retrovirus probe under stringent washing conditions and is capable of producing human-serum-resistant RVP and wherein said vectors, either singly or collectively, express a cellular targeting protein and retroviral gag and pol genes in amounts sufficient to package said RVP; and

(b) recovering said packaging cell line.

2. The method of Claim 1, wherein said cell line is the Mpf cell line designated by ATCC accession number 1656-CRL.

3. The method of Claim 1, wherein said cell line is α -galactosyl positive.

4. The method of Claim 1 or 2, wherein said cellular targeting protein is an amphotropic retroviral env protein, a xenotropic retroviral env protein, a polytropic retroviral env protein, a JSRV env protein, vesicular stomatitis virus G protein or transferrin.

5. A packaging cell line produced by the method of Claim 1 or 2.

6. A method for preparing a stable, retroviral producer cells capable of producing human serum-resistant retroviral vector particles (RVP) which comprises

(a) introducing a retrovirus vector into the packaging cell line of Claim 1, wherein said retrovirus vector is capable of being packaged into an RVP and comprises a heterologous gene capable of expression in a human; and

(b) recovering said producer cells.

7. The method of Claim 6, wherein said cells are Mpf cells designated by ATCC accession number 1656-CRL.

5 8. The method of Claim 6, wherein said cells are α -galactosyl positive.

9. The method of Claim 6, wherein said cellular targeting protein is an amphotropic retroviral env protein, a xenotropic retroviral env protein, a polytropic retroviral env protein, a JSRV env protein, vesicular stomatitis virus G protein or transferrin.

10

10. Producer cells prepared by the method of Claim 6 or 7.

11. A method for preparing human serum-resistant retroviral vector particles (RVP) which comprises:

15 (a) introducing a retrovirus vector into the packaging cell line of Claim 1, wherein said retrovirus vector is capable of being packaged into an RVP and comprises a heterologous gene capable of expression in a human;

20 (b) culturing said cell line for a time and under conditions sufficient to produce said RVP; and

(c) recovering said RVP.

12. The method of Claim 11, wherein said cell line is the Mpf cell line designated by ATCC accession number 1656-CRL.

25

13. The method of Claim 11, wherein said cell line is α -galactosyl positive.

14. The method of Claim 11 or 12, wherein said cellular targeting protein is an amphotropic retroviral env protein, a xenotropic retroviral env protein, a polytropic retroviral env protein, a JSRV env protein, vesicular stomatitis virus G protein or transferrin.

30

15. The method of Claim 12 wherein said cell line produces RVP having a supernatant titer on mink cell line Mv-1-Lu of at least about 10^4 to about 10^8 colony forming units per milliliter.

35

16. A method for preparing human serum-resistant retroviral vector particles (RVP) which comprises:

(a) culturing the producer cells of Claim 6 for a time and under conditions sufficient to produce said RVP;
5 and

(c) recovering said RVP.

17. The method of Claim 16, wherein said cells are α -galactosyl positive.

18. The method of Claim 16, wherein said cellular targeting protein is an amphotropic retroviral env protein, a xenotropic retroviral env protein, a polytropic retroviral env protein, a JSRV env protein, vesicular stomatitis virus G protein or transferrin.

19. The method of Claim 16 wherein said cell line produces RVP having a supernatant titer on mink cell line Mv-1-Lu of at least about 10^4 to about 10^8 colony forming units per milliliter.

20. Retroviral vector particles produced by the methods of any one of Claims 11, 12, 16 or 41.

21. Retroviral vector particles prepared from the producer cells of Claim 10.

22. A method for transducing a cell with a retroviral vector in the presence of a body fluid which comprises administering the retroviral vector particles (RVP) of Claim 20 to said cell.

23. The method of Claim 22, wherein said RVP is administered to said cell *ex vivo* or *in vivo*.

24. The method of Claim 23, wherein said RVP is administered *in vivo* by aerosol, transmucosal, oral, intravenous, intraperitoneal, intramuscular, transdermal, intradermal, subdermal, transmucosal or intrathecal delivery.

25. A method of gene therapy which comprises delivering a therapeutic molecule encoded on a retrovirus vector to a human cell via retroviral vector particles (RVP) of Claim 20.

26. The method of Claim 25 wherein said therapeutic molecule is a hormone, a growth factor, an enzyme, a lymphokine, a cytokine, a receptor, an angiogenic factor, or an anti-angiogenesis factor.

5 27. The method of Claim 25, wherein said RVP is administered to said cell *ex vivo* or *in vivo*.

28. The method of Claim 27, wherein said RVP is administered *in vivo* by aerosol, transmucosal, oral, intravenous, intraperitoneal, intramuscular, transdermal, 10 intradermal, subdermal, transmucosal or intrathecal delivery.

29. A method for transducing a cell with a retroviral vector in the presence of a body fluid which comprises administering the retroviral vector particles 15 (RVP) of Claim 21 to said cell.

30. The method of Claim 29, wherein said RVP is administered to said cell *ex vivo* or *in vivo*.

31. The method of Claim 30, wherein said RVP is administered *in vivo* by aerosol, transmucosal, oral, 20 intravenous, intraperitoneal, intramuscular, transdermal, intradermal, subdermal, transmucosal or intrathecal delivery.

32. A method of gene therapy which comprises delivering a therapeutic molecule encoded on a retrovirus 25 vector to a human cell via retroviral vector particles of Claim 21.

33. The method of Claim 32 wherein said therapeutic molecule is a hormone, a growth factor, an enzyme, a lymphokine, a cytokine, a receptor, an angiogenic 30 factor, or an anti-angiogenesis factor.

34. The method of Claim 32, wherein said RVP is administered to said cell *ex vivo* or *in vivo*.

35. The method of Claim 34, wherein said RVP is administered *in vivo* by aerosol, transmucosal, oral, 35 intravenous, intraperitoneal, intramuscular, transdermal,

intradermal, subdermal, transmucosal or intrathecal delivery.

5 36. A method for transferring a heterologous gene into a human cell which comprises contacting said human cell with the producer cells of Claim 10 under conditions such that said producer cells release RVP containing a retrovirus vector encoding said heterologous gene and thereby introducing said gene into said human cell.

10 37. The method of Claim 36, wherein said producer cells are implanted in a human.

 38. The method of Claim 37, wherein said producer cells are implanted in a human brain.

 39. A pharmaceutical composition comprising the RVP of Claim 20 and a pharmaceutically acceptable carrier.

15 40. A pharmaceutical composition comprising the RVP of Claim 21 and a pharmaceutically acceptable carrier.

 41. The method of Claim 16, wherein said cells are Mpf cells designated by ATCC accession number 1656-CRL.